Whole body diffusion-weighted magnetic resonance imaging in the diagnosis of recurrent ovarian cancer: a clinical feasibility study

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ABSTRACT

Objectives: To assess the clinical feasibility of whole body diffusion-weighted magnetic resonance imaging (WB-DWI/MRI) for diagnosis and prediction of complete tumour resection in patients with suspected recurrent ovarian cancer.

Methods: Fifty-one women clinically suspected for ovarian cancer recurrence underwent 3-Tesla WB-DWI/MRI in addition to contrast-enhanced computed tomography (CT). WB-DWI/MRI was assessed for detection of tumour recurrence, -prediction of tumour extent and complete resection compared to CT. Tumour presence was confirmed by pathology obtained by surgery or biopsy, or by imaging follow-up.

Results: WB-DWI/MRI showed 94% accuracy for detecting ovarian cancer recurrence, compared to78% for CT (p=0.008). WB-DWI/MRI showed better sensitivity (Sens (%) [95% CI]) than CT for detecting involvement of surgically-critical tumour sites including mesenteric root infiltration (92 [62-100] versus 31 [10-61]), small bowel (93 [64-100] versus 21 [6-51]),colon carcinomatosis (91 [57-100] versus 27 [7-61]) and irresectable distant metastases (90 [54-99] versus 20 [4-56]). WB-DWI/MRI correctly predicted complete resection in 33 of 35 (94%) patients eligible for salvage surgery compared 17 of 35 (49%) for CT ($p<0.001$).

Conclusions: WB-DWI/MRI allowed better detection of ovarian cancer recurrence and better prediction of complete resection compared to CT.

Advances in knowledge: WB-DWI/MRI could assist in optimizing treatment planning for recurrent ovarian cancer, particularly by improving patient selection for salvage surgery, thus giving eligible patients the highest chance on prolonged survival and refraining patients who would not benefit from extensive surgery reducing related morbidity and mortality.

INTRODUCTION

Despite continuing improvement of treatment of ovarian cancer patients, up to 85% of these women will develop tumour recurrence.[1-4] While debulking surgery is well accepted for treatment of primary ovarian cancer, the surgical management of recurrent disease remains controversial due to lack of major supporting prospective data and lack of well-defined operability criteria that may predict complete resection. A recent multicentre trial (DESKTOP II) prospectively developed the 'Arbeitsgemeinschaft Gynaekologische Onkologie' (AGO-) score providing a clinical tool to select patients for salvage surgery.[5] Complete resection at primary surgery, good performance status and absence of ascites represented a likelihood of 76% for secondary debulking to no residual tumour.[5] However, eligibility for salvage surgery largely depends on accurate and timely detection of tumour recurrence and accurate description of total tumour extent. The role of computed tomography (CT) and 18-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET)/CT for the detection of recurrent ovarian cancer has been established. However, their value for predicting complete resection remains controversial, because commonly disease load is underestimated.[5-7] Diffusion-weighted MRI (DWI) distinguishes itself from conventional MRI sequences by the ability to detect water molecule displacements at a cellular scale (in the order of 10–30 μm) allowing functional

characterization of tissue microstructural properties. The signal intensity of lesions depends on the amount of impediment of the movement of water molecules. The more water molecule movement is restricted in tissues (e.g. tumoral lesions), the brighter lesions appear at heavily diffusion-weighted images (b = 1000 s/mm²), in contrast to the suppressed background tissue, ascites and blood vessels.[8] The combination of this high contrast-ratio, spatial resolution in the order of millimetres, robust performance, and short imaging times allows DWI to depict small tumour deposits in large body volumes in a clinically time-efficient way. For primary ovarian cancer, studies with abdominal and whole body diffusion-weighted MRI (WB-DWI/MRI) have indicated high sensitivity for detecting metastases allowing to predict incomplete resection.[9-11] The purpose of this study was to assess the clinical feasibility of WB-DWI/MRI for diagnosis of patients with suspected recurrent ovarian cancer and prediction of complete tumour resection.

METHODS AND MATERIALS

Patients

Between July 2011 and June 2013, patients clinically suspected for recurrent ovarian cancer were prospectively and consecutively enrolled. The local ethics committee approved this study and all patients provided written informed consent. Inclusion criteria were (1) suspicion of recurrent ovarian cancer based on clinical symptoms (eg. bloating, pelvic or abdominal pain, diarrhoea or constipation), clinical examination (including gynaecological ultrasound) and/or increase of cancer antigen (CA)-125 and (2) Complete resection and completion of all chemotherapy cycles during primary treatment. Patients with contra-indications to MRI (eg. pacemaker, claustrophobia, MRI incompatible devices or implants) were excluded. All patients underwent WB-DWI/MRI in addition to the clinical CT scan and imaging data were read blinded to other imaging and clinical/biochemical results.

At the oncologic board, patients were first decided on their clinical eligibility for salvage surgery based on the presence or absence of medical comorbidities, complicated primary surgery with abscesses or fistulisation preventing major surgery and the DESKTOP II criteria including Primary R0 resection, good performance status, absence of ascites.[12] In these patients, operability was then decided on the imaging appearance of disease spread

according to institutional surgical criteria, with disease spread compromising surgery consisting of distant irresectable metastases, carcinomatosis of the duodenum, stomach, pancreas, large vessels of the coeliac trunk and hepatoduodenal ligament, metastases behind the portal vein, diffuse serosal small bowel or colon carcinomatosis or deep tumoral involvement of the superior mesenteric artery and mesenteric root.[12] In case of conflicting WB-DWI/MRI and CT findings for recurrence detection or operability assessment potentially compromising curative treatment correlative invasive or imaging diagnostic tests were performed prior to treatment decision (Figure 1).

CT scanning

Breath-hold contrast-enhanced CT (Sensation 16, Sensation 64, Definition Flash, Siemens Medical Systems, Erlangen, Germany) was obtained, 90 minutes after per-oral contrast ingestion [30 ml iodinated contrast agent (Telebrix Gastro, Guerbet), 300 mg/ml, in 900 ml water], chest scan 17 s and abdomen scan 90 s after intravenous contrast injection [120 ml iodinated contrast agent (Visipaque, GE Healthcare); 320 mg/ml]. The following parameters were used: pitch 1.2 /s, rotation speed 0.5 s, slice thickness 5 mm, slice gap 1 mm and collimation 0.6 mm. The reference tube voltage was set at 120 kV

and the reference current was 200 mAs for the abdomen and 110 mAs for the thorax using automated Care Dose software.

WB-DWI/MRI scanning

Three Tesla WB-DWI/MRI (Ingenia, Philips Healthcare, Best, The Netherlands) was performed with parallel radiofrequency transmission and phased-array surface coils. Free-breathing WB-DWI/MRI was acquired in four imaging stations in the transverse plane at b=0 and b=1000 s/mm^2, covering head to pelvis using the following parameters: short-T1-inversion-recovery (STIR) prepulse for fat suppression with inversion time (TI) of 250 ms, b-values in three orthogonal directions of 0 and 1000 s/mm² with automated calculation of apparent diffusion coefficient maps, parallel imaging factor of 2.5, repetition time (TR) of 8454 ms, echo time (TE) of 67 ms, slice thickness of 5 mm, intersection gap of 0.1 mm, field of view (FOV) of 420 x 329 mm, acquired voxel size of 4.57 x 4.71 mm with a reconstructed voxel size of 2.19 x 2.16 mm. The number of signal averages (NSA) was 2 for the thorax (with 2 averages for b=0 and 6 for b=1000 s/mm²) and 1 (with 1 average for b=0 and 3 for b=1000 s/mm²) for all other stations. The number of slices was 45 for the head and neck imaging station and 50 for the other imaging stations. Multiplanar reformatted axial, coronal and sagittal WB-DWI/MRI images were

reconstructed from the transverse b1000 images and combined into a single stack of WB-DWI/MRI images with a slice thickness of 5 mm.

Coronal free breathing single shot Turbo spin-echo (SS-TSE) T2-weighted and breath-hold abdominal-pelvic and thoracic gadolinium-enhanced (Dotarem®, Guerbet, Roissy, France) 3D T1-weighted gradient-echo sequences were used as anatomical reference. Coronal SS-TSE T2-weighted images were acquired in 3 imaging stations with parallel imaging factor of 2, TR/TE of 3000/87 ms, slice thickness of 6 mm, interslice gap op 0.6 mm, FOV of 375 x 447 mm, parallel imaging factor of 4 and 35 slices for all stations. 3D T1-weighted gradient-echo sequences of the pelvis and abdomen were acquired with parallel imaging factor of 2, TR/TE of 3.6/1.25-2.20 ms, slice thickness of 1.5 mm, 90 slices, FOV 375 x 304 mm, acquired voxel size of 1.49 x 1.50 mm and reconstructed voxel size of 0.71 x 0.71 mm with 1 NSA. Coronal abdominal mDIXON was acquired with identical imaging parameters except for a FOV of 400 and 352 slices. Finally, a twenty seconds breath-hold eTHRIVE of the chest was acquired with identical parameters as the mDIXON sequences except for a TR/TE of 3.2/1.5 ms, 148 slices and reconstructed voxel size of 0.98 x 0.97.

Patients drank one litre of pineapple juice two hours before the WB-DWI/MRI and were administered an antispasmodic (butylhyoscine, 20 mg IV) to improve the assessment of the small bowel serosa. Total scanning time was 38 minutes.

CT image interpretation

An abdominal radiologist with 12 years of experience interpreted the CT. Peritoneal metastases were recorded when there was nodular, infiltrative or confluent thickening and/or contrast-enhancement over the peritoneal surfaces, omentum or mesentery. Involvement of the bowel serosa was recorded in case of bowel masses, thickening or contrast-enhancement of the bowel wall.

Nodal metastases were characterized based on morphological features indicating necrosis and short-axis diameter (1 cm threshold for abdominal lymphadenopathies and 0.5 cm threshold for thoracic lymphadenopathies).[13] Pathologically enhancing masses in the liver, lung, or pleura were recorded as distant metastases.[14]

WB-DWI/MRI image interpretation

An abdominal radiologist with 10 years of experience interpreted the WB-DWI/MRI combining the information of b1000 DW images and anatomical sequences. Peritoneal

metastases were recorded when there was nodular, infiltrative or confluent b1000 hyperintensity and/or contrast enhancement over the peritoneal surfaces, omentum or mesentery. Involvement of the bowel serosa was recorded in case of b1000 and/or contrast-enhancing bowel masses, nodular or infiltrative thickening of the bowel wall. Lymph nodes were qualitatively assessed based on shape and b1000 signal intensity; lymph nodes showing (heterogeneous) higher b1000 signal intensity compared to surrounding lymph nodes were considered malignant.[9] Distant metastases were identified based on increased b1000 signal not attributable to physiologically impeded diffusion or T2 shine-through.[15]

Reference standard

Exploration during laparotomy or laparoscopy with pathology was the primary reference standard. In case of suspected distant or retroperitoneal nodal metastases critical towards salvage surgery, image-guided biopsy or fine needle aspiration cytology was performed. If surgical or histopathological correlation was impossible, correlative FDG-PET/CT and/or imaging follow-up with consecutive CT or MRI scans for at least 6 months was used as reference standard. All imaging, surgical and pathological reports used identical disease site labelling to facilitate proper correlation. The following imaging criteria were

applied as reference standard in absence of surgical or histopathological correlation: assessed lesions with FDG uptake not attributable to physiological or inflammatory uptake at correlative FDG-PET/CT, appearing significantly larger (≥20% increase) during follow-up or showing a significant decrease (≥30%) under chemotherapy were considered true positive. Lesions detected at imaging but negative at correlative FDG-PET/CT or resolving without therapy were considered false positive. Sites described negative at imaging, showing negative correlative FDG-PET/CT or follow-up were considered true negative. Lesions undetected at imaging, but positive at correlative FDG-PET/CT or showing significant increase (≥20%) during follow-up were considered false negative.

Data analysis

STATISTICA 9.1 software (Statsoft Inc, Tulsa, OK, USA) was used with *P* values below 0.05 indicating statistical significance. CT and WB-DWI/MRI were compared for detection of tumour recurrence per patient; for assessment of tumour extent in sites critical towards surgery including according to institutional surgical criteria as mentioned above and for assessment of operability with the aim for resection to no residual tumour.[12] Descriptive statistical data for WB-DWI/MRI and CT (sensitivity and specificity with

95% binomial confidence intervals (CI), Clopper-Pearson) were determined per patient and for surgically critical sites. Per-patient statistical differences between WB-DWI/MRI and CT for detection of recurrence and operability assessment were examined with two-tailed McNemar tests.

RESULTS

Patients

Fifty-six women were included. After excluding 5 patients without surgical correlation or follow-up, 51 were analysed (median age 63, range 33-84 years). For all patients, Initial FIGO stage, histology, primary treatment, diagnosis-to-recurrence interval as well as CA-125 and presence of ascites at time of suspected recurrence are summarized in Table 1.

Figure 1 summarizes the clinical and therapeutic management of patients and use of standard reference. Ovarian cancer recurrence was confirmed in 48/51 (94%). In 3 patients tumour recurrence was excluded (explorative laparotomy and tumour-free imaging follow-up during 1 year in 2 patients and tumour-free imaging follow-up during 1 year in 1 patient) (Figure 2).

In 13 patients no attempt for surgery was performed: one patient presented with negative imaging findings, even on correlative FDG-PET/CT but became progressive under

imaging follow-up; two patients refused surgery, 5 patients were randomised in the DESKTOP III chemotherapy arm and 5 patients had poor performance status (Figure 2). Imaging follow-up was used for correlation of initial findings on WB-DWI/MRI and CT. Thirty-five patients were considered eligible for surgery, based on clinical criteria alone. Seventeen of these 35 (49%) of patients underwent salvage debulking surgery with 15 reaching resection to no residual tumour and two being inoperable at laparotomy. Eighteen of these 35 patients (51%) were deferred from surgery based on imaging assessment of disease load (Figure 2). The discordant cases between CT and WB-DWI/MRI (9/18, 50%), were assessed with laparoscopy for correlation of peritoneal disease in three patients, (endoscopic) ultrasound guided biopsy or fine needle aspiration cytology in 4 patients (one suprarenal, one left supraclavicular, one mediastinal lymphadenopathy and one pleural metastasis) and FDG-PET/CT in two patients (one suprarenal and one mediastinal lymphadenopathy).

Detection of ovarian cancer recurrence

WB-DWI/MRI correctly identified 47/48 (98%) patients with confirmed tumour recurrence with 94% accuracy compared with 40/48 (83%) for CT showing 78% accuracy

(*p*=0.008) (Table 2). In the three patients negative for tumour recurrence, WB-DWI/MRI was false positive in 2 and CT in all 3 patients.

Disease extent critical for surgery: WB-DWI/MRI versus CT

Table 2 shows comparative sensitivity and specificity with 95% CI of WB-DWI/MRI and CT for assessing disease extent critical for surgery following the institutional operability criteria.[12] WB-DWI/MRI showed higher sensitivity for detecting confluent or multifocal carcinomatosis of the mesenteric root, the small bowel and colon compared with CT (Figure 3). In addition, WB-DWI/MRI had higher sensitivity for detecting irresectable metastases compared to CT (Figure 4).

Prediction of -complete resection: WB-DWI/MRI versus CT

In the 35 patients clinically eligible for salvage surgery, WB-DWI/MRI correctly predicted operability in 33 of 35 (94%) of patients versus 17 of 35 (49%) for CT (*p*<0.001).

In 18 of 35 (51%) patients, WB-DWI/MRI predicted inability of complete resection. Findings of diffuse peritoneal disease and/or distant metastases were concordant with CT findings in 9 of 18 (50%) patients and confirmed during further follow-up under systemic

treatment. In the other 9 of 18 (50%) patients WB-DWI/MRI predicted inoperability in patients regarded as operable by CT findings (Figure 2). The inoperability was confirmed either by laparoscopy, image guided biopsy or correlation with FDG-PET/CT in all 9 patients. Compared to CT, WB-DWI/MRI correctly detected diffuse intestinal serosal spread in three patients, suprarenal or supradiaphragmatic subcentimetric lymphadenopathies in 5 patients and pleural metastases in one patient.

In 17 of 35 (49%) patients, WB-DWI/MRI predicted complete resection. Complete resection was possible in 15 of 17 (88%) patients while disease extent was underestimated in two (12%) patients found inoperable at start of salvage debulking surgery. In comparison, CT only predicted complete resection in 8 of 17 (47%), underestimated disease extent in the two (12%) patients found inoperable at start of salvage debulking surgery and wrongly assigned 7 patients as unable to reach resection to no residual tumour (Figure 2).

DISCUSSION

In this prospective study, WB-DWI/MRI showed higher accuracy than CT for detection of recurrent ovarian cancer and enabled better prediction of operability with the aim for complete resection. The better prediction of operability by WB-DWI/MRI over CT was mainly attributable to the higher sensitivity for detection of multifocal or diffuse serosal intestinal disease spread, metastases around the central mesenteric vessels and irresectable distant metastases.

The diagnostic accuracy of 94% for identifying patients with recurrent ovarian cancer by WB-DWI/MRI in our study is similar with results of a recent publication where whole body MRI with DWI sequence detected recurrence of gynaecological tumour in 23 of 25 (92%) included patients.[16] Previous studies investigating the feasibility of MRI for detection of ovarian cancer recurrence have yielded variable results with sensitivity ranging between 57 to 90% and specificity between 33 and 100%.[17] Using abdominal Gadolinium-enhanced MRI alone, Low RN et al found 90% sensitivity, 88% specificity and 89% accuracy for detecting recurrent or persistent ovarian cancer after cytoreductive surgery, even in patients with normal CA-125.[18] Balestreri et al found 84% sensitivity and 100% specificity using combined T2-weighted and Gadolinium-enhanced MRI for

detecting recurrent ovarian cancer in patients with rising tumour marker and negative thoraco-abdominal CT.[19] However, contrary to our study, older reports and a meta-analysis found no significant differences when comparing MRI and CT for detecting recurrent ovarian cancer.[17, 20, 21] Besides lower sample sizes, a number of included studies in the meta-analysis were performed with different MRI techniques that lacked breath-hold imaging, fat saturation for contrast-enhanced imaging and DWI-sequences. Substantial advances in MRI technology enabling fast breath-hold fat-saturated Gadolinium-enhanced imaging and particularly the addition of a (whole body) DWI-sequence are factors that have substantially improved sensitivity for detection of peritoneal and lymph node metastases.[17, 20-22] This probably explains the improved detection of tumour recurrence and higher accuracy of WB-DWI/MRI over CT in our study.

More than its ability for detecting tumour recurrence, WB-DWI/MRI outscored CT for prediction of complete resection. The better prediction of operability by WB-DWI/MRI over CT in our study is in line with a report in primary ovarian cancer where abdominal DWI/MRI allowed prediction of suboptimal surgery with 90% accuracy.[11] In our study, WB-DWI/MRI correctly predicted operability in 94% of patients clinically eligible for salvage surgery. The substantially better detection of disease sites critical for surgery -

predominantly multifocal or diffuse serosal intestinal metastases, metastases around the central mesenteric vessels and irresectable distant metastases - was the main contributor to the better performance for operability assessment by WB-DWI/MRI over CT in our study. By large, this is explained by the superior contrast resolution of DWI for depiction of peritoneal and nodal/distant metastases over CT, particularly in the absence of ascites, in the bowel mesentery and serosa or in subcentimetric lymph nodes.[9, 22, 23]

Previously, doubt was cast on the diagnostic capacity of stand-alone WB-DWI/MRI for detection of recurrent gynaecological tumour, presumably by the impeding effects of post-therapeutic fibrosis and tissue scarring.[16] However, radiological-pathological correlation in treated head and neck cancer has shown that the low cellular density and large interstitial space of fibrosis corresponded with low signal intensity on high b-value DWI-images, while the hypercellularity and restricted interstitial space in tumour recurrence resulted in increased signal intensity in on high b-value DWI-images. As such, DWI allows to differentiate recurrent tumour from treatment induced fibrosis or inflammation irrespective of anatomical or metabolical imaging findings.[24]

The ability for precise diagnosis of recurrent cancer by DWI was confirmed in two studies, evaluating DWI for assessment of recurrent pelvic cancer. Lambregts et al found that the addition of DWI to the conventional MRI protocol reduced the number of false

positives by 20% and improved interobserver agreement, thereby improving radiologist confidence.[25] In that study, all 8 patients with equivocal CT findings in this study were correctly diagnosed by DWI/MRI suggesting superior sensitivity and specificity for DWI/MRI over CT. Kitajima et al showed that DWI had significantly better sensitivity and accuracy relative to T2-weighted MRI with equal performance as contrast-enhanced MRI in 62 patients with suspected intrapelvic recurrence of gynaecological cancers.[26] Importantly, adding DWI allowed better detection of metastatic disease sites other than the suspected site of tumour recurrence allowing better description of total disease extent which may be useful for surgical planning.

Accordingly, in our study, the better description of total disease extent and improved sensitivity for small tumoral deposits enabled WB-DWI/MRI to better identify patients with peritoneal disease spread, lymphadenopathies or distant metastases beyond surgical reach compared to CT and thus better identify patients who would not benefit from salvage surgery due to incomplete resection. Contrary, the better differentiation of tumour recurrence from post-treatment tissue distortions, particularly mesenteric infiltration not attributable to tumour, enlarged reactive lymph nodes and liver lesions allowed WB-DWI/MRI to better predict complete resection compared to CT, the latter wrongly

assigning 7 patients as having peritoneal or distant lymphadenopathies/metastases beyond surgical reach.

While optimal salvage debulking surgery may improve median survival, its success depends on early detection of recurrence and thorough patient selection.[27] In order to optimize patient selection, clinical predictive score models including the AGO score and the model of Tian have been validated to overcome current radiological limitations for predicting complete resection.[28] In the DESKTOP II study - validating the AGO-score - half of the patients had far more peroperative tumour load than predicted by imaging and in one quarter of the patients disease load was overestimated by imaging, while the AGO-score correctly predicted complete resection in 76% of patients.[5, 29] However, as a drawback, the AGO-score is currently not designed to predict inoperability in negatively-scored patients.[5, 29] Also, while both models have high positive predictive value for complete resection of 82% and 80. 3% respectively, they suffer from relatively high false negative rates 68.5% and 55.6% respectively.[28] It is currently unclear whether diagnostic laparoscopy could enhance the predictive value of both models, bearing in mind an associated morbidity rate of 1-5%.[28, 30, 31] The high accuracy of WB-DWI/MRI of 94% for predicting operability and ability to identify both patients with under- and

overestimated disease load by CT suggests its potentially additional value to clinical predictive models for operability assessment in patients with recurrent ovarian cancer.

This study has some limitations. Firstly, direct surgical or pathological correlation was not available for all disease sites. However, laparoscopy or -tomy in patients in whom surgery was not indicated was considered non-ethical and meticulous imaging follow-up was used instead. As per study design, lesions considered critical for surgical planning were confirmed by biopsy or laparoscopy.

Secondly, the patient population with direct surgical correlation was relatively small. However, this is inherent to the design of a single-centre pilot study for which only a selected number of patients are eligible for salvage surgery. Therefore the results of this study need to be validated in larger study populations.

Thirdly, we did not compare the results of WB-DWI/MRI with FDG-PET/CT. Not all patients with suspected recurrent ovarian cancer receive routine clinical FDG-PET/CT in our centre due to its reported relatively low performance to predict complete resection.[5] Nevertheless, future comparative studies are warranted to elucidate the potential synergistic value of microstructural and metabolic imaging, especially in the advent of the development of hybrid PET/MRI.[16]

Last, we did not assess interobserver agreement. However, a recent study showed good interobserver agreement using similar interpretation criteria.[9]

In conclusion, WB-DWI/MRI showed high accuracy, superior to CT, for detection of ovarian cancer recurrence and prediction of complete resection in patients with clinical symptoms or increase of tumour marker. WB-DWI/MRI particularly improved the non-invasive assessment of multifocal or diffuse serosal intestinal tumour spread, metastatic deposits around the central mesenteric vessels and irresectable distant metastases. Our study suggests that WB-DWI/MRI could substantially improve clinical management and patient selection for salvage surgery pending validation in larger studies.

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TABLES

Table 1 Patient demographics

		n (%)
Median age (y)	*63 (range, 33-84)*	
Initial FIGO stage*		
Borderline		*1 (2)*
I		*3 (6)*
II		*4 (8)*
III		*31 (61)*
IV		*7 (14)*
Unknown		*5 (10)*
Histology		
Serous papillary adenocarcinoma		*36 (71)*
Adult granulosa cell tumour		*5 (10)*
Clear cell carcinoma		*2 (4)*
Serous cystadenocarcinoma		*2 (4)*
Endometrioid carcinoma		*1 (2)*
Sertoli-Leydig cell tumour		*1 (2)*
Borderline mucinous tumour		*1 (2)*
Dysgerminoma (immature teratoma)		*1 (2)*
Carcinosarcoma		*1 (2)*
Unknown		*1 (2)*
Primary treatment		
Primary debulking surgery		*38 (75)*
R0 resections**		*38 (100)*

Interval debulking surgery after neoadjuvant chemotherapy	*13 (25)*
R0 resections	*12 (92)*
Rest < 1cm	*1 (8)*
Diagnosis-to-recurrence interval (months)	
Median (min-max)	*31 (range, 5-285)*
Pre-operative CA-125[***]	
> 35 U/mL	*29 (57)*
< 35 U/mL	*19 (37)*
unknown	*3 (6)*
Ascites	
No ascites	*43 (84)*
Limited ascites	*5 (10)*
Moderate ascites	*1 (2)*
Severe ascites	*2 (4)*

[*]*FIGO, International Federation of Gynaecology and Obstetrics;*

[**]*R0 resection, complete resection;*

[***]*CA-125, Cancer Antigen-125*

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Table 2 Comparative sensitivity and specificity for detection of recurrent disease and disease extent according to operability criteria between CT and WB-DWI/MRI

		Sens[a] (%) TP/(TP+FN)	95% CI[c] LL[d] (%)	95% CI UL[e] (%)	Spec[b] (%) TN/(TN+FP)	95% CI LL (%)	95% CI UL (%)
Detection of recurrent disease							
Detection of recurrence	WB-DWI/MRI	98 (47/48)	89	100	33 (1/3)	1	91
	CT	83 (40/48)	70	93	0 (0/3)	0	71
Peritoneal carcinomatosis							
Superior mesenteric artery involvement	WB-DWI/MRI	100 (2/2)	20	100	100 (49/49)	91	100
	CT	50 (1/2)	3	97	100 (49/49)	91	100
Diffuse infiltration of mesenteric root of small bowel	WB-DWI/MRI	92 (12/13)	62	100	97 (37/38)	85	100
	CT	31 (4/13)	10	61	100 (38/38)	89	100
Diffuse and confluent carcinomatosis of stomach	WB-DWI/MRI	100 (6/6)	52	100	100 (45/45)	90	100
	CT	50 (3/6)	14	86	96 (43/45)	84	99
Diffuse and confluent carcinomatosis of small bowel	WB-DWI/MRI	93 (13/14)	64	100	95 (35/37)	80	99
	CT	21 (3/14)	6	51	95 (35/37)	80	99
Intrahepatic M+	WB-DWI/MRI	100 (1/1)	5	100	100 (50/50)	91	100
	CT	0 (0/1)	0	95	92 (46/50)	80	97
Infiltration of large vessels of lig.[f] hepatoduodenale	WB-DWI/MRI	100 (6/6)	52	100	100 (45/45)	90	100
	CT	33 (2/6)	6	76	100 (45/45)	90	100
Metastases behind the porta hepatis	WB-DWI/MRI	100 (7/7)	56	100	98 (43/44)	86	100
	CT	29 (2/7)	5	70	98 (43/44)	86	100
Multifocal or confluent carcinomatosis of colon	WB-DWI/MRI	91 (10/11)	57	100	98 (39/40)	85	100
	CT	27 (3/11)	7	61	100 (40/40)	89	100
Distant metastases							
Resectable inguinal lymph nodes	WB-DWI/MRI	100 (1/1)	5	100	98 (49/50)	88	100
	CT	100 (1/1)	5	100	96 (48/50)	85	99

Solitary resectable retrocrual or paracardial nodes	WB-DWI/MRI	100	(1/1)	5	100	100	(50/50)	91	100
	CT	100	(1/1)	5	100	98	(49/50)	88	100
Irresectable distant metastases	WB-DWI/MRI	90	(9/10)	54	99	100	(41/41)	89	100
	CT	20	(2/10)	4	56	98	(40/41)	86	100

[a]*Sens, sensitivity;*

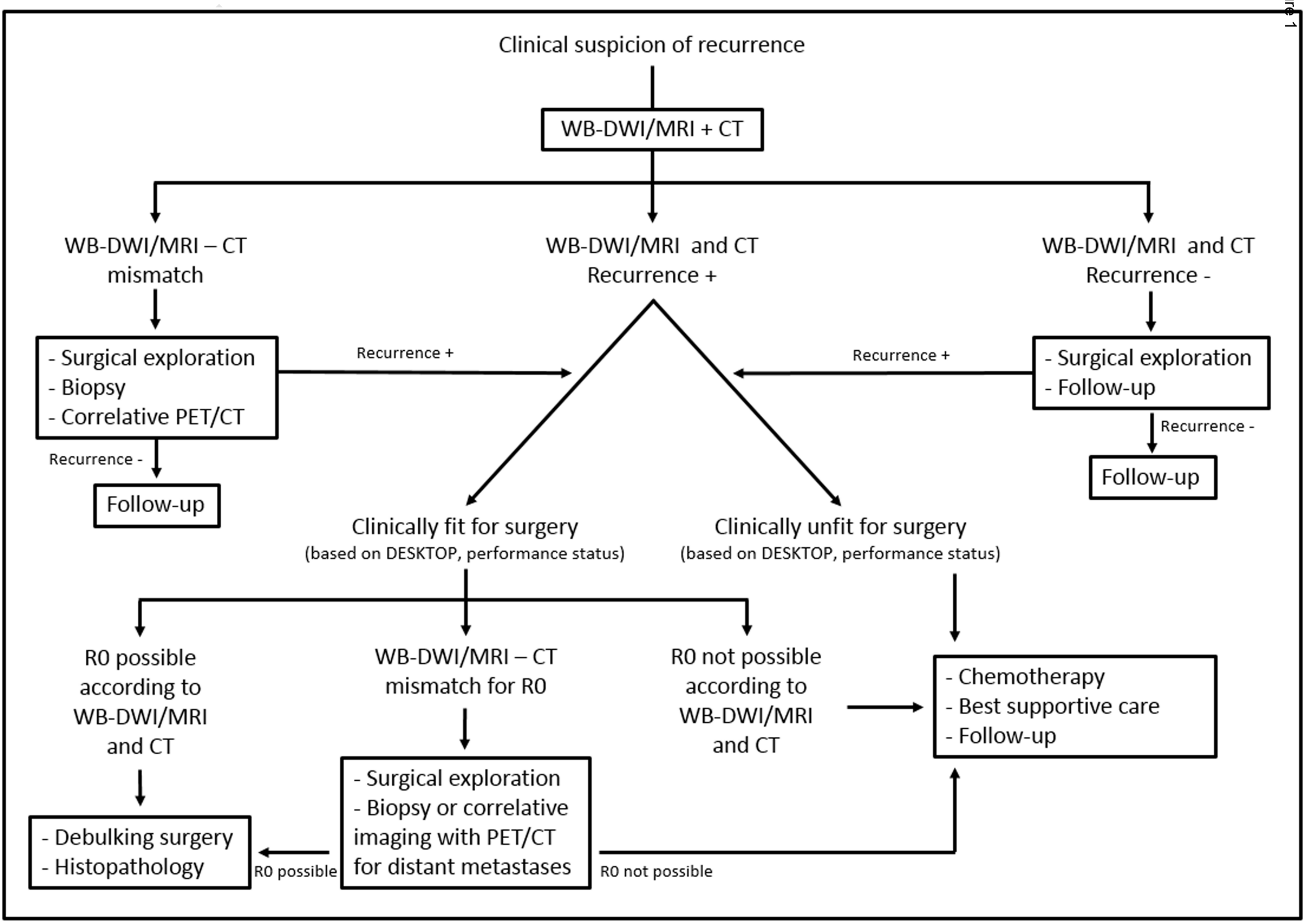
[b]*Spec, specificity;*

[c]*95% CI, 95% binomial confidence interval (Clopper-Pearson);*

[d]*LL, lower limit;*

[e]*UL, upper limit;*

[f]*lig., ligamentum;*


Clinical suspicion of recurrence
WB-DWI/MRI + CT
WB-DWI/MRI – CT mismatch
WB-DWI/MRI and CT Recurrence +
WB-DWI/MRI and CT Recurrence -
- Surgical exploration
- Biopsy
- Correlative PET/CT
Recurrence +
Recurrence +
- Surgical exploration
- Follow-up
Recurrence -
Recurrence -
Follow-up
Follow-up
Clinically fit for surgery
(based on DESKTOP, performance status)
Clinically unfit for surgery
(based on DESKTOP, performance status)
R0 possible according to WB-DWI/MRI and CT
WB-DWI/MRI – CT mismatch for R0
R0 not possible according to WB-DWI/MRI and CT
- Chemotherapy
- Best supportive care
- Follow-up
- Debulking surgery
- Histopathology
R0 possible
- Surgical exploration
- Biopsy or correlative imaging with PET/CT for distant metastases
R0 not possible

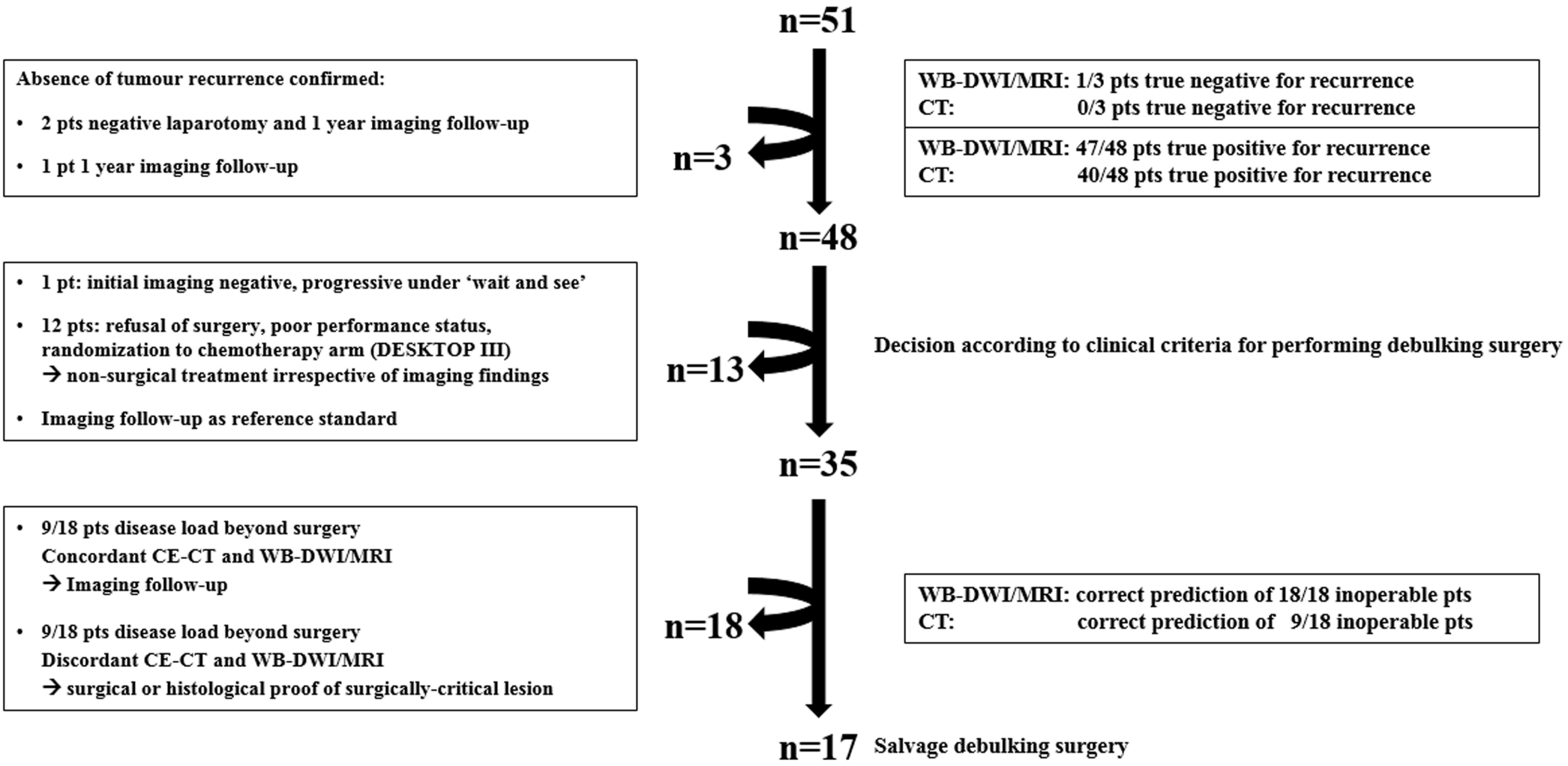

n=51
Absence of tumour recurrence confirmed:
• 2 pts negative laparotomy and 1 year imaging follow-up
• 1 pt 1 year imaging follow-up
n=3
WB-DWI/MRI: 1/3 pts true negative for recurrence
CT: 0/3 pts true negative for recurrence
WB-DWI/MRI: 47/48 pts true positive for recurrence
CT: 40/48 pts true positive for recurrence
n=48
• 1 pt: initial imaging negative, progressive under 'wait and see'
• 12 pts: refusal of surgery, poor performance status, randomization to chemotherapy arm (DESKTOP III)
→ non-surgical treatment irrespective of imaging findings
• Imaging follow-up as reference standard
n=13
Decision according to clinical criteria for performing debulking surgery
n=35
• 9/18 pts disease load beyond surgery
Concordant CE-CT and WB-DWI/MRI
→ Imaging follow-up
• 9/18 pts disease load beyond surgery
Discordant CE-CT and WB-DWI/MRI
→ surgical or histological proof of surgically-critical lesion
n=18
WB-DWI/MRI: correct prediction of 18/18 inoperable pts
CT: correct prediction of 9/18 inoperable pts
n=17
Salvage debulking surgery
• 15 pts resection to no residual tumour (R0)
• 2 pts inoperable
WB-DWI/MRI: correct prediction of R0 resection in 15/17 pts
CT: correct prediction of R0 resection in 8/17 pts

Figure 3

Click here to download Figure Figure3.tif

Figure 4

Click here to download Figure Figure4.tif

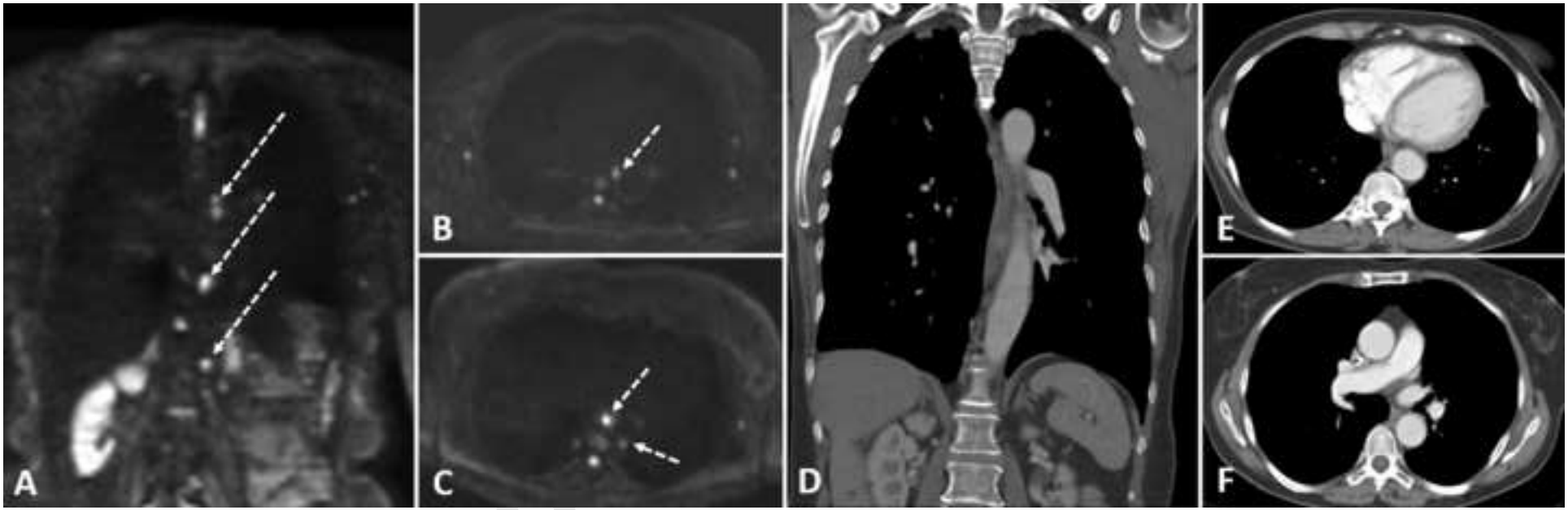


Figure 1: Flowchart describing the process of clinical decision making towards salvage surgery following the imaging results; any case of conflicting imaging results that would potentially defer eligible patients from possible salvage surgery was correlated by either surgical exploration, biopsy of the surgically-critical suspect lesion or correlative imaging.

Figure 2: Clinical and therapeutic management of patients and use of standard reference.

Figure 3: Sixty-eight-year-old woman with previously treated stage IV serous papillary ovarian cancer shows increased serum CA-125. WB-DWI/MRI shows carcinomatosis of the stomach, small bowel and colon and peritoneal metastases depicted as diffuse linear or nodular b1000 hyperintensity of the serosal surfaces (arrows) (A, B, E, F) in correlation to T2-weighted imaging (C). CT was interpreted as negative (D, G, H). Lesion progression at imaging follow-up during six months confirmed peritoneal carcinomatosis.

Figure 4: Seventy-one-year-old woman with previous history of high grade serous papillary ovarian carcinoma with increased serum CA-125. Whole body DWI/MRI shows b1000 strongly hyperintense mediastinal lymph nodes suspect for lymphadenopathies (dashed arrows) (A, B, C), interpreted as negative at CT (D, E, F). Cytology after endoscopic fine-needle aspiration confirmed these nodal metastases.